GENERAL THORACIC SURGERY

PLEURAL SPACE IRRIGATION AND MODIFIED CLAGETT PROCEDURE FOR THE TREATMENT OF EARLY POSTPNEUMONECTOMY EMPYEMA

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Objective: **The incidence of postpneumonectomy empyema is 5% to 10%. Approximately half of postpneumonectomy empyemas occur within 4 weeks of pneumonectomy. A bronchopleural fistula is found in more than 80% of the patients. The classic treatment of postpneumonectomy empyema includes parenteral antibiotics, drainage of the pleural space, removal of necrotic tissue, and open pleural packing for many weeks followed by obliteration of the empyema space with antibiotic fluid or muscle. This approach results in prolonged hospitalization, repeated operations, and significant morbidity. As a possible means of decreasing morbidity with the classic treatment of postpneumonectomy empyema, we studied the use of pleural space irrigation in these patients.** ***Method:*** **In a 5-year period, we treated 22 patients with early postpneumonectomy empyema. All patients had a bronchopleural fistula. All patients underwent emergency drainage of the pleural space followed by thoracotomy, debridement of necrotic tissue, closure of the bronchial stump with absorbable monofilament suture, and pleural space irrigation. After a negative Gram stain from the pleural fluid, the pleural space was filled with 2 L of debridement antibiotic solution (DAB solution) (gentamicin 80 mg/L, neomycin 500 mg/L, and polymyxin B 100 mg/L), and the irrigation and drainage catheters were removed.** ***Results:*** **Twenty patients had negative Gram stains on day 9, and 2 patients had a negative Gram stain on day 16. The mean duration of hospitalization was 12.9 ± 3.4 days. There was no recurrence of empyema or a bronchopleural fistula.** ***Conclusions:*** **Pleural space irrigation followed by obliteration of the pleural space with an antibiotic solution required one surgical procedure and resulted in significantly shorter hospitalization and decreased morbidity in patients with early postpneumonectomy empyema. (J Thorac Cardiovasc Surg 1998;116:943-8)**

Postpneumonectomy empyema (PNE) occurs in 5% of patients after standard pneumonectomy and 10% after completion pneumonectomy.[1-5] Approximately half of the PNEs occur early, within the first 2 to 4 weeks of the original procedure. In modern series, the mortality of PNE with bronchopleural fistula (BPF) has been 11% to 13%.[6,7] A BPF is found in more than 80% of patients with PNE and in virtually all patients with early PNE.[8] The treatment of early PNE includes (1) adequate pleural drainage, (2) closure of the BPF, and (3) obliteration of the residual pleural space.[9] In practice, these principles translate into surgical drainage of

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the pleural space, closure of the BPF, removal of necrotic tissue, and open pleural packing for many weeks followed by obliteration of the empyema space with antibiotic fluid or vascularized tissue. Although this approach has been successful in up to 92% of cases, it results in prolonged hospitalization, repeated operative procedures, and significant morbidity.[10] To decrease the morbidity associated with the classic treatment of PNE, we explored the use of closed pleural space irrigation followed by obliteration of the pleural space with an antibiotic solution in patients with early PNE.

Patients and methods

Between July 1992 and July 1997, 22 patients with early PNE, within 4 weeks of pneumonectomy, were treated by one of us (F.G.). Eighteen patients were referred from outside institutions. Four patients had undergone a pneumonectomy at our institution. The patients with early PNE had a cough with expectoration of serosanguineous fluid, a radiograph showing lowering of the fluid level in the evacuated hemithorax, and bronchoscopic evidence of a BPF. All patients with early PNE underwent emergency chest tube thoracostomy in the supine position and drainage of the pleural space. The patients underwent intubation with a double-lumen endotracheal tube and the BPF was approached via a posterolateral thoracotomy on the ipsilateral side. The BPF was identified by positive-pressure ventilation. The remaining bronchus was dissected by meticulous sharp dissection, which was maintained immediately adjacent to the bronchial wall to minimize potential injury to the adjacent vessels or the esophagus. Frozen sections of the bronchial and peribronchial tissue were obtained to rule out malignancy at the resection margin. Care was taken to achieve a final bronchial stump length of approximately 1 cm or less and to preserve the peribronchial tissue proximal to the site of transection to maximize collateral blood flow. The bronchial stump was then closed with 4-0 monofilament absorbable suture. The pleural space was meticulously debrided. Pleural space irrigation was instituted by placing 2 large flexible drainage catheters through stab wounds in the second intercostal space and tunneling in a Z fashion into the chest. One catheter was placed overlying the mediastinum, and the other was placed onto the posterolateral chest wall. Two 32F chest tubes were placed anteriorly and posteriorly and brought out through a Z-shaped tunnel in the seventh intercostal space. The thoracotomy incision was closed with absorbable monofilament suture in multiple layers. Care was taken to obtain a water-tight closure. The skin was closed with interrupted mattress sutures of 3-0 nylon, and deep retention mattress sutures of 1-0 nylon were placed intermittently to decrease the tension on the skin closure. The pleural space was irrigated with 0.1% povidone-iodine solution (Betadine; 40 mL/h) for 7 days. On day 8, the povidone-iodine irrigation was discontinued and the pleural space was irrigated with normal saline solution (40 mL/h) for 24 hours. On day 9, a Gram stain of the chest tube drainage fluid was obtained. If the Gram stain was positive for organisms or leukocytes, povidone-iodine irrigation was resumed and continued for days 9 through 15, followed by saline solution irrigation on day 16 and a second Gram stain on day 17. This cycle was continued until a negative Gram stain was obtained. With a negative Gram stain the pleural space was filled with 2 L of DAB solution (gentamicin 80 mg/L, neomycin 500 mg/L, and polymyxin B 100 mg/L), and the irrigation and drainage catheters were removed.

All patients underwent culture-specific antimicrobial therapy until the removal of the drainage catheters. All patients received enteral alimentation either orally or with the use of nasoduodenal feeding tubes. After discharge from the hospital, the patients were followed up with chest radiographs and blood tests at 7 days and 1 month and with chest computed tomographic scans at 6 months and 1 year.

Bronchoscopy was performed in patients in whom a recurrent BPF was suspected.

Results

Eighteen patients were referred from outside institutions. During the 5-year period of the study, 4 of 163 patients (2.5%) had an early PNE after a pneumonectomy in our institution. There were 16 men and 6 women (mean age 62 ± 5 years). Eighteen patients had undergone a right pneumonectomy and 4 had a left pneumonectomy. Two patients with bronchiectasis had completion pneumonectomy. Twenty patients had undergone pneumonectomy for lung cancer. The predisposing factors for early PNE were obstructive pneumonitis,[12] steroid therapy,[3] preoperative radiation therapy,[3] malnutrition,[2] and bronchiectasis.[2] In addition to these risk factors, a long bronchial stump was seen in 17 patients at the time of the surgical exploration. In all patients the bronchial stump opening was less than 25% of the diameter of the bronchus. After day 8 of pleural space irrigation, 20 patients had negative Gram stains. In 2 patients irrigation was continued until day 16, at which time the Gram stain was negative. The mean hospitalization time was 12.9 ± 3.4 days. At the time of discharge, all patients were fully functional. One patient had a prolonged nonproductive cough, but bronchoscopic study failed to show a fistula and the cough resolved after 6 weeks. At 3 and 6 months' follow-up, the response rate remained 100%. At 1 year, neither PNE nor BPF had recurred. Twelve patients (55%) were followed up for greater than 3 years without recurrence of the BPF.

Discussion

The first reported pneumonectomy, which was performed by Graham and Singer[11] in 1933, was compli-

cated by a BPF on the ninth postoperative day. In the 1940s and 1950s the rate of BPF after a pneumonectomy was 20% to 30%, with a mortality of 60%.[12-15] At present the rate of BPF after a pneumonectomy has decreased by one half.[15] After a pneumonectomy a BPF invariably results in an empyema. The mortality of PNE with a BPF has been reported to be 11% to 13%.

Many preoperative factors increase the risk of PNE. Increased age and male sex increase the incidence.[16] The majority of our patients were elderly men. Preoperative radiation is a risk factor, presumably by decreasing the vascular supply to the bronchus. Three patients in our series had undergone preoperative radiotherapy. Poor preoperative nutritional state and the use of steroids can impede healing and increase the risk of BPF. Five patients in this series either were malnourished or were on a regimen of prolonged steroid therapy. Active infection in the form of resection in the face of inflammatory conditions, bronchiectasis, presence of postobstructive pneumonitis, gross contamination of the pleural space, and sputum cultures positive for tuberculosis increases the risk of PNE.[17-19] Fourteen patients in the present report had either postobstructive pneumonitis or bronchiectasis.

Technical factors also play a significant role in increasing the risk of PNE. A long bronchial stump can be the site of stagnation of sputum and breakdown as the result of secondary infection. Residual tumor and devascularization of the bronchial stump and excessive tension on the bronchial closure can lead to breakdown of the stump and PNE.[18-20] In 17 of the 22 patients, a long bronchial stump was seen at re-exploration.

The best means of decreasing the morbidity and mortality associated with BPF is prevention. The bronchial stump needs to be handled carefully. Excessive length and devascularization of the stump should be avoided. In patients with predisposing risk factors, the bronchial stump should be reinforced with vascularized tissue in the form of the omentum, pericardial fat pad pedicle, or chest wall muscle. After prevention, a high index of suspicion and an aggressive approach to the diagnosis play a significant role in decreasing the morbidity and mortality of PNE.

The management of PNE has ranged from tube thoracostomy to open pleural drainage to thoracoplasty.[20-24] Unfortunately many of the approaches in the past have ignored the well-established rules for the treatment of any infected space. Furthermore, the treatment protocols have not accounted for a potential difference in the pathophysiology of early versus late PNE. In 1963, a landmark paper by Clagett and Geraci[22] described a technique for the management of PNE that was based on sound surgical principles for the treatment of an abscess. The 2-stage procedure consisted of open pleural drainage, closure of the BPF, removal of the necrotic tissue, and secondary closure or obliteration of the pleural cavity with antibiotic solution. The Clagett procedure has been reported to be effective in 88% of patients, with failures resulting from persistent or recurrent BPF.[21] In an attempt to address these failures, Pairolero and Arnold[24] described the transposition of well-vascularized extrathoracic muscle as an intermediate step before obliteration of the pleural cavity with antibiotic solution. This modification of the "Clagett" procedure was designed to further reinforce the bronchial stump and to decrease the size of the pleural cavity. The success of the Pairolero modification of the "Clagett" procedure has been 83.9%.[7] The Pairolero modification remains our procedure of choice for late PNE. Although this procedure is associated with excellent success, it requires prolonged hospitalization, repeated dressing changes and operations, and significant morbidity.

Pleural space irrigation has been advocated as an alternate means of treating empyema and pneumonectomy space infection.[25,26] Although this technique has had reasonable promise, it has been hampered by the lack of a uniform approach, small groups of patients, a varied patient population, and high failure rates. In an attempt to decrease the morbidity and hospitalization for the subset of patients with early PNE, we explored the technique of pleural space irrigation as a further modification of the "Clagett" procedure. We hypothesized that the most likely cause of early PNE is a combination of technical errors in handling the bronchus or the result of delayed healing from the predisposing factors. It would follow then that a technically satisfactory reclosure of the bronchus, debridement of the acutely infected pleural space, and control of contamination by an irrigation system may be comparable to open packing and mechanical control of the contaminated space. Inasmuch as there was no recurrence of BPF or empyema, pleural space irrigation followed by obliteration of the pleural space with an antibiotic solution may represent an ideal treatment option for patients with early PNE with a small BPF. This modification of the Clagett procedure requires 1 surgical procedure and results in significantly shorter hospitalization and decreased morbidity in this selected subset of patients with PNE.

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Discussion

Dr Peter C. Pairolero *(Rochester, Minn).* PNE, with or without BPF, has always been associated with significant morbidity and mortality. The authors' 1-year success of 100% is indeed outstanding and better than any previously published. It is important to remember, however, that all postpneumonectomy BPFs are associated with an empyema and that management is based on the well-established rules for treatment of any infected space, that is, the infection must be drained, any fistula closed, and the space obliterated. Each of these 3 areas has a treatment spectrum and obviously the end result is the aggregate of each treatment option.

First, successful drainage of an infected pleural space is dependent on the age of the infection. Those empyemas that are only a few days old are associated with an effusion that is more a transudate than an exudate. As a result, simple tube drainage is effective and the addition of pleural space irrigation, while generally not necessary, certainly facilitates healing. In contrast, when the empyema is a few weeks old, the effusion is thick, tenacious, and associated with a woody, indurated pleura. Simple drainage and irrigation in this chronic situation simply does not work. Instead, debridement is necessary to remove the exudate before healing of the pleura can begin.

Dr Gharagozloo, can you describe in greater detail for us what the local conditions may be that may want to force you into leaving an open window. I believe it is more than just the age of the empyema.

Second, of the 3 things, BPFs can range in size from those so small that they cannot be visualized to those that involve the entire width of the bronchus. Simple drainage of an early empyema with a pinhole fistula will heal the fistula in every case. In contrast, if the bronchus has dehisced at the level of the carina, a complete suture reclosure may be impossible without some type of tissue reinforcement.

Third, the pleural space must be obliterated if the fistula is to eventually heal. Dr Jim Clagett in his report to this Association in 1963, clearly demonstrated, and we all have come to follow, that obliteration with antibiotic solution has been the method of choice. In the authors' collective review, the fistulas were small, the empyemas early, and the cavities obliterated with antibiotic solution. One would predict that the results would be excellent, but 100% is indeed outstand-

ing. However, I still want to caution that larger BPFs associated with older empyemas may not fare as well.

Dr Gharagozloo. Thank you for your comments, Dr Pairolero. The answer to your question rests in the quality of the tissues. When I was a fellow under you, I learned that lesson and I think it is a very important point: If you find woody, indurated tissue on opening the patient, you should not institute the irrigation system. In many of these patients, a simple mechanical debridement followed by the combination of the povidone-iodine irrigation, which is also an antibiotic as well as a mechanical system, works quite well. However it is the experience of the surgeon in picking which patients should be treated in which way that makes the difference.

Dr Joseph S. Ladowski *(Fort Wayne, Ind).* I would like to offer a caution and ask one question. Our tertiary care referral center has cared for far fewer of these patients in a similar fashion, and we have seen a patient go from mild renal dysfunction to dialysis dependence with the installation of 160 mg of gentamicin plus a gram of neomycin into the pleural space. That is the caution.

The question is this: Have you quantified the absorption of these very nephrotoxic antibiotics from the pleural space? Perhaps if the fluid is truly Gram stain negative you may want to use systemic antibiotics instead.

Dr Gharagozloo. I appreciate the comments. We have learned over the years that systemic antibiotics probably do not have a major role in dealing with this situation. This is a local situation that needs to be treated in a local fashion.

As far as the placement of DAB solution in the pleural space, certainly there can be absorption. We have not looked at it. I think that's well established, that there is absorption and certainly that risk is there. The other risk is with the irrigation system. As you know, we have gone down to significantly lower levels of povidone-iodine because of the povidone-iodine toxicity that is seen with mediastinal irrigation systems and so forth.

I agree with the cautions. In our experience, when we check the Gram stain on these patients, the organisms seem to be a hodgepodge because of the presence of a BPF. Trying to do specific organism-focused treatment by intravenous antibiotics would probably not be wise in this setting.

Dr Walter Klepetko *(Vienna, Austria).* If you assume that the irrigation system has contributed significantly to your success and you are irrigating with an amount of 40 mL/h, one would expect that the fluid is only in the posterior part of the chest. Do you think it is important that it is distributed all over the thoracic cavity? In that case do you request that your patients frequently change their position?

In our limited experience with a similar procedure, we have also had success in a patient who had already had 2 surgical attempts at closure of a large bronchial stump fistula. In that patient we found a very thick pleura, and we found it essential to take all the pleura off, as in an extrapleural pneumonectomy, with all the necrotic tissue. How aggressively are you performing the debridement?

Dr Gharagozloo. We are talking about early PNE. A patient with a condition such as you described would not be treated in this way, because that patient would need repeated debridement by mechanical means and basically the various other modifications of Clagett procedure. I would term that patient's condition *late PNE*. Even if the presentation were early, as Dr Pairolero mentioned, the time is not important; it is what the surgeon sees in the pleural space that is important. That is key.

I have often wondered whether higher amounts of this irrigation system would be better, because it would obviously distribute better throughout the pleural space. That would be an interesting study to do if we had the patients with whom to do it.

The 40 comes from the experience with the mediastinum. We try to put these catheters in the mediastinum in the back of the chest such that there are many holes and all of the chest basically bathes with this fluid. However, I think a higher level might be better. That would be something to check out in the future.

Dr Klepetko. Deriving from a small experience with 4 cases of late PNE treated in a similar way, I think you should be more confident in your method, and I think you could also use it in late PNE.

Dr Gharagozloo. Thank you.

Dr Joseph I. Miller, Jr *(Atlanta, Ga).* You have just described the most extensive experience ever reported with the best success rate in the treatment of early PNE. When this was originally reported by Dr Clagett with Dr Geraci in 1966 and then later reported by Stafford in the mid-80s from the Mayo Clinic, their success rate there was 76%. They reported that if you had a single organism you had a much higher success rate than if you had a mixed organism, particularly if you had a Gram negative organism.

I am not sure that I can understand how you achieved a 100% success rate when Dr Pairolero and the others and I have been trying for 25 years to obliterate the problem. I would ask 3 questions.

To what do you attribute your success when, despite all the efforts of others, no one has been able to attain that?

Second, the original Clagett solution was BAN, Bacitracin, Aerosporin, and neomycin. You've used the acronym DAB. I understand the concentrations are lower, but I am curious about DAB, because your drugs are gentamicin, neomycin, and polymyxin B. Have you had any problems with the toxicity?

Dr Gharagozloo. Thank you for your comments. If you look at Dr Clagett's paper and then the subsequent papers that he published, the reason the Clagett procedure failed was that the bronchus broke down; there was a recurrence of a BPF that made things fail. Dr Pairolero's modification of that procedure is very much meant to deal with that problem, which is to put a vascularized muscle on top so that the bronchus does not fall apart; if you look at that, the numbers get better.

One key in our procedure was that we switched from using polypropylene (Prolene; Ethicon, Inc, Somerville, NJ), which

is what I had learned and used in the years previous to this study, to something that is absorbed so there is no material in the pleural space that is foreign and perhaps acts to cause infection. Another key is to close that bronchus and to deal with these patients very early.

DAB is a term that I carry with me from the Mayo Clinic. It stands for debridement antibiotic solution.

Dr Victor F. Trastek *(Rochester, Minn).* I have 2 questions. What role do you think the negative Gram stain plays? If you do not get a negative Gram stain after 2, 3, or 4 weeks, what do you do?

Dr Gharagozloo. In that case we would convert to the typical operation—open packing and so forth.

Dr Trastek. You would not continue with closed treatment if the Gram stain remained positive?

Dr Gharagozloo. No, I do not think that would be appropriate.

Dr Stanley C. Fell *(Bronx, NY).* You have just said that you use an absorbable suture, but in the text you say a nonabsorbable monofilament suture. What suture do you use? What is the brand name?

Dr Gharagozloo. It is absorbable suture, it is monofilament, and it is PDS polydioxanone (Ethicon).